MCKEE, VOORHEES & SEASE, PLC

ATTORNEYS AT LAW

801 GRAND AVENUE • SUITE 3200 • DES MOINES, IA 50309-2721
PHONE: 515-288-3667 • FAX: 515-288-1338 • www.ipmvs.com

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DATE: April __1__, 2004

TO: Art Unit 1631
             Examiner Marjorie A. Moran

COMPANY: USPTO

PHONE:

FAX: **703-872-9306**

FROM: **John D. Goodhue**

NUMBER OF PAGES (Including cover):   6

COMMENTS: Please file the attached RESPONSE TO RESTRICTION REQUIREMENT:

APPLICANT :   MARANAS et al.
SERIAL NO :   10/043,440
FILED   :   January 10, 2002
TITLE   :   METHOD AND SYSTEM FOR MODELING
                 CELLULAR METABOLISM

Grp./A.U. :   1631
Examiner   :   MORAN, Marjorie A.
Conf. No. :   1336
Docket No. :   P05468US01

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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SUPPLEMENTAL RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Mail Stop Non-Fee Amendment
Alexandria, VA 22313-1450

Sir:

This is a response to the Office Communication dated March 17, 2004.

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CERTIFICATE OF MAILING/TRANSMISSION (37 CFR 1.8(a))
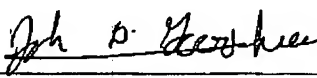
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Date: ___April 1, 2004___   ___[signature]___
                                              JOHN D. GOODHUE

Amendments to the Claims

Claim 1 (Original):   A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model;

applying constraints to the flux balance analysis model, the constraints selected from the set

consisting of: qualitative kinetic information constraints, qualitative regulatory

information constraints, and differential DNA microarray experimental data constraints.

Claim 2 (Original):   The method of claim 1 wherein the constraints are logic constraints

selected to protect against violation of a kinetic or regulatory barrier.

Claim 3 (Original):   The method of claim 1 wherein the constraints are connectivity restraints.

Claim 4 (Original):   The method of claim 1 further comprising the step of applying mixed-

integer linear programming to solve for a desired metabolic outcome.

Claim 5 (Original):   The method of claim 1 further comprising the step of solving for a desired

metabolic outcome.

Claim 6 (Original):   A method for modeling cellular metabolism of an organism that improves

upon a flux balance analysis model, comprising:

constructing the flux balance analysis model; and

applying a plurality of logic constraints to the flux balance analysis model.

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Claim 7 (Original):   The method of claim 6, further comprising selecting the set of logic

constraints to protect against violation a kinetic or regulatory barrier.

Claim 8 (Original):   The method of claim 6 wherein the logic constraints are defined by a

relationship between changes in reaction fluxes and metabolic concentrations.

Claim 9 (Original):   The method of claim 6 wherein the logic constraints are defined by

a relationship between reaction fluxes and transcript levels of gene coding.

Claim 10 (Original):   The method of claim 6 wherein the logic constraints are represented by

binary variables.

Claim 11 (Original):   The method of claim 10 wherein a first binary variable represents the

presence of a reaction and a second binary variable represents the absence of a reaction.

Claim 12 (Original):   The method of claim 6 further comprising applying a computational

procedure to identify a minimal set of metabolic reactions.

Claim 13 (Original):   The method of claim 12 further comprising selecting a growth rate, and

wherein the step of applying a computational procedure is applying a computational procedure to

identify the minimal set of metabolic reactions capable of supporting the growth rate.

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Claim 14 (Original):   The method of claim 6 further comprising the step of applying mixed-integer linear programming to solve for a desired metabolic outcome.

Claim 15 (Original):   The method of claim 6 further comprising the step of solving for a desired metabolic outcome.

Claim 16 (Original):   The method of claim 15 further comprising engineering a change in an organism based on the desired metabolic outcome.

Claim 17 (Original):   A method for determining a reduced genome, comprising:

selecting a minimal set of reactions from a set of metabolic reactions that meets a growth rate

    target;

mapping enzymes catalyzing the minimal set of reactions to a corresponding set of coding genes,

    the corresponding set of coding genes defining a reduced genome.

Claim 18 (Original):   The method of claim 16 wherein the growth rate target is a biomass target production rate.

Claim 19 (Original):   A system for modeling cellular metabolism of an organism, comprising:

a flux balance analysis model;

a plurality of constraints applied to the flux balance analysis model, the constraints selected from

    the set consisting of: qualitative kinetic information constraints, qualitative regulatory

    information constraints, and differential DNA microarray experimental data constraints.
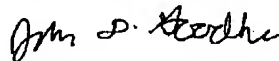
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REMARKS

The Examiner states the reply filed on January 9, 2004, was not fully responsive to the prior Office Action because the Applicant did not elect a species, as set forth on page 3 of the Office Action mailed on December 15, 2003. The Applicant elects species drawn to (A) changes in reaction fluxes and metabolic concentrations.

The Applicant has previously elected Group I claims 1-16 and 19. The Examiner has previously found claims 1-7, 10-16, and 19 to be generic and therefore readable upon the elected species. The Applicant further submits that claim 8 is also readable on the elected species.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

John D. Goodhue (signature)

JOHN D. GOODHUE, Reg. No. 47,603
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No: (515) 288-3667
Fax No: (515) 288-1338
CUSTOMER NO: 27407

Attorneys of Record

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